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## Case report

## A case of Granulomatosis with Polyangiitis presenting with significant ocular cicatricial scarring and symblepharon formation



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## ABSTRACT

**Purpose:** To report a case of Granulomatosis with Polyangiitis presenting with rare findings of cicatricial entropion progressing to significant symblepharon and fornix obliteration.

**Observations:** An otherwise healthy patient with initial presentation findings of lower lid entropion with minimal cicatricial changes and a corneal ulcer. Management with an entropion Jones procedure repair produced good early postoperative results. 2 months post entropion repair, this patient represented with rapid progression to severe corneal ulceration, symblepharon formation and total obliteration of lower fornix and near complete obliteration of upper fornix of the left eye with concurrent acute kidney injury. He fulfilled diagnostic criteria for Granulomatosis with Polyangiitis (GPA). Systemic immunosuppressive treatment with prednisone and cyclophosphamide allowed acute kidney injury to recover however progressive cicatricial scarring ensued.

**Conclusions and importance:** Cicatricial entropion is a very rare presentation of GPA which can take years to progress however with surgical intervention, rapid recurrence and severe tarsal-conjunctival disease progression can ensue despite systemic immunosuppressive therapy. To prevent such unexpected surgical complication, we recommend a thorough systemic evaluation prior to consideration of lid surgery in any cases of cicatrizing conjunctivitis presentation.

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## 1. Introduction

Granulomatosis with polyangiitis (GPA), formerly known as Wegner's granulomatosis, is a rare systemic inflammatory disease affecting small to medium size blood vessels, with an estimated annual incidence of 5–10 cases per million people.<sup>1</sup> Historically a fatal disease if untreated, recognition of disease activity is critical for treatment initiation, as early organ damage is a predictor of poor outcome.<sup>2,3</sup> GPA belongs to the group of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides, of which microscopic polyangiitis (MPA) and Churg-Strauss syndrome (CSS) also belong. Several diagnostic criteria exist (American college of Rheumatology, Chapel Hill Consensus Conference, European Medicines Agency)<sup>4–6</sup> for classification of these similar groups of diseases. Ophthalmologic manifestations have been reported across all the ANCA associated vasculitides however, these most commonly occur in GPA patients, where up to half of the cases may develop eye

involvement.<sup>7,8</sup> Such ocular presentations are diverse, ranging from more common orbital disease, conjunctivitis, scleral/episcleral disease, to corneal ulceration, uveitis, retinal vasculitis, optic neuropathy, orbital masses and nasolacrimal duct involvement.<sup>7,9</sup> Of the rarer presentations reported in the literature, GPA causing cicatricial scarring has been reported in only a handful of cases.<sup>10–12</sup> Here we report a case of GPA presenting with cicatrizing disease causing entropion and significant symblepharon formation.

## 2. Case report

An 84 year old male presented with a 2 month history of left eye irritation and decreased visual acuity. His past ocular history included a left cataract extraction 3 years previously, further complicated by a dislocation of IOL requiring a vitrectomy and IOL exchange. On the right side he has had a previous penetrating eye injury, with resulting aphakia after repair. Right corrected visual acuity was 6/18 however, our patient was not using corrective lenses for this eye.

On presentation to our clinic, findings included a mildly inflamed left eye with visual acuity reduced from 6/9 to 6/36.

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There was lower lid entropion, trichiasis and some conjunctival scarring. Associated with these changes was an inferior corneal ulcer with a few anterior chamber cells. Fundal examination was not possible. There were no complaints or acute findings with his right eye and he otherwise denied being generally unwell at the time.

Initial management involved topical chloramphenicol ointment and entropion temporised with tape. He subsequently underwent a left lower lid entropion repair (Jones Procedure) 5 days later. Topical antibiotics and lubrication were continued postoperatively. Post-operative reviews were conducted weekly for the first month, with the 4th week follow-up showing good left lower lid position with a reasonable fornix and complete healing of the corneal ulcer. Mild left upper lid swelling was noted then, with suspicious trichiatric eyelashes epilated. Further review at 10 weeks post-op was planned to assess the recovery.

Within the same week of the planned 10 week review, we received a referral from our patient's family doctor requesting an urgent Ophthalmology review as now there was a new history of left eye pain, further decreased visual acuity and a recent 8 day hospital admission to another regional hospital where he was treated for acute kidney injury thought secondary to hypovolaemia.

Prompt review of our patient now showed significant new ulceration of the left lower lid margin with total obliteration of the lower fornix and symblepharon formation (Fig. 1). There was also a new corneal ulcer with inferior corneal melt. An initial diagnosis of an inflammatory process was made and topical antibiotics and topical prednisolone were commenced. He was admitted for further investigation as the suspicion was an underlying systemic vasculitic cause.

Detailed medical workup for admission revealed a history of chronic sinusitis pre dating surgery however from about 2 weeks post-surgery, progressive post nasal drip and blood stained mucus, together with lethargy and a 15 kg weight loss was recalled by the patient. Examination also showed right nostril scarring and clots.

Investigations included blood results of white blood cells  $9.5 \times 10(9)/L$  (WBC), normal eosinophils, CRP 89 mg/L, creatinine 165  $\mu\text{mol/L}$ , ANCA positive, antinuclear antibody (ANA) negative, anti-proteinase 3 antibody (PR3) of 507 units/ml, anti-myeloperoxidase antibody (MPO) of 6 units/ml, red blood cells (RBC) and albumin in urine and an unremarkable chest X-ray. Renal biopsy showed pauci-immune crescentic glomerulonephritis. MRI orbits showed a slightly asymmetrical enlarged left lacrimal gland, asymmetric increased T2 signal and contrast enhancement left

eyelid as well as above left globe extending medially and mucosal thickening of the right maxillary sinus (Fig. 2).

The clinical presentation and results suggested the underlying cause was GPA with renal, upper respiratory and ocular involvement and as such, systemic prednisone, cyclophosphamide and prophylactic cotrimoxazole were subsequently commenced under multidisciplinary care. Over the following 3 months on systemic therapy, renal function normalised, inflammatory markers and PR3 antibodies decreased and topical steroids were subsequently stopped after the initial 2 weeks. Some initial ocular improvement was noted, with reduction in amount of adhesions, healing of the corneal ulcer and ulcerated lid margins however at the most recent review some 4 months after initiation of systemic therapy, the left lower lid symblepharon remains with complete obliteration of the fornix and extensive corneal scarring resulting in hand motions only vision in the left eye (Fig. 3).

Both verbal and written informed consent was given from the patient for use of case medical photography for publication purposes.

### 3. Discussion

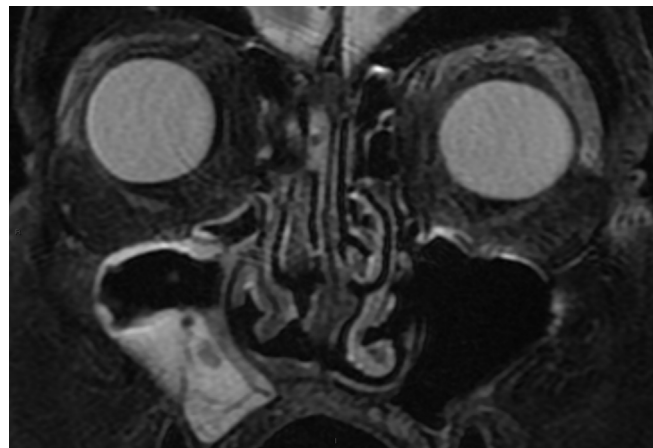
Under the 1990 American College of Rheumatology criteria for classification for GPA, our patient fulfils two positive criteria of nasal inflammation and kidney microhaematuria.<sup>4</sup> Such respiratory and biopsy confirmed kidney involvement, combined with positive ANCA, PR3 and negative MPO, certainly makes a diagnosis of GPA in our patient.<sup>13</sup> Conjunctival biopsy was not performed in this case as consideration of the risk of inducing further trauma and inflammation was deemed rather high compared to any further benefits a tissue diagnosis might have added at the time.

Literature review of ocular manifestations of GPA typically report non-specific conjunctivitis affecting 16–18% of GPA patients.<sup>7,8,10</sup> Robinson et al. has further in detail described tarsal-conjunctival disease to include conjunctival hyperaemia, granulomatous lesions, necrosis, fibrovascular proliferation, fibrous scar, corneal involvement and trichiasis/entropion.<sup>10</sup>

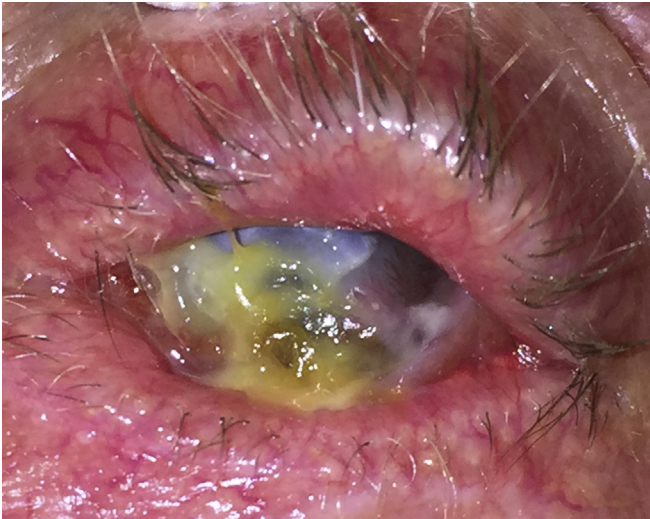
To date, only 6 cases of GPA causing cicatricial entropion have been reported and of these, one patient developed symblepharon formation, another with fibrovascular proliferation extending over the pupillary axis and a third patient with both of the aforementioned features.<sup>10,14</sup> Our case demonstrates a severe presentation of these rare GPA findings, with early cicatricial entropion developing



**Fig. 1.** Left lower lid margin ulceration with symblepharon formation and inferior corneal melt 2 months after entropion repair.



**Fig. 2.** T2 weight magnetic resonance imaging of the orbits showed asymmetric increased signal and contrast enhancement left eyelid as well as above left globe extending medially and mucosal thickening of the right maxillary sinus.



**Fig. 3.** Progressive left eye conjunctival and corneal scarring with lower fornix obliteration 4 months after systemic immunosuppressant therapy.

into complete obliteration of the fornix and symblepharon formation. Of note, our patient did undergo an entropion repair approximately 10 weeks prior to representation and establishment of GPA diagnosis. With very few cases, limited conclusions can be made regarding the role of medical and surgical intervention in such cases. Robinson et al. does report one patient who underwent excision of fibrovascular tissue over the cornea which had been slowly progressive over 20 months. Despite systemic prednisone over the perioperative period, this patient developed rapid disease recurrence with the fibrovascularisation process entering the pupillary axis within 3 months. Described also within this study was a second patient where systemic prednisone and methotrexate did not alter the progressive fibrovascular tissue growth and entropion formation over a course of 3 years.<sup>10</sup> Meier et al. reports a case of cicatrizing conjunctivitis where no systemic therapy was initiated but treatment consisted of blepharitis regime (including topical steroids). This patient also had progressive tarsal scarring and cicatrizing entropion over the following 2 years.<sup>11</sup>

Despite our patient being initiated on systemic immunosuppressant therapy when GPA diagnosis was confirmed, review 4 months later continued to show extensive corneal and conjunctival scarring with symblepharon and fornix obliteration. Our case shows similarity to the findings of Robinson et al., whom noted that in their small number of cases, tarsal-conjunctival disease activity was largely unaffected by systemic immunosuppressive therapy.<sup>10</sup> With or without systemic therapy, cicatricial entropion and fibrovascular changes tended to progress over years<sup>10,11</sup> however rapid recurrence occurred within the one previously reported patient with surgical excision and certainly in our own case, ocular disease progression was rapid with severe fornix scarring and corneal ulceration. The extent and rapidity of disease activity in our patient does pose further questions regarding potential predictors of visual outcome. Our patient represented during an acute episode of systemic inflammation and had not previously been initiated on systemic treatment, as well as recent surgical intervention for entropion. With comparison to the patient receiving surgical intervention in Robinson et al., it is plausible that further traumatic insult resulting in increased site inflammation could have a role in rapidity of disease recurrence and progression. Such is an observation made in this inflammatory disease where the underlying pathophysiology is still not fully understood. Similarly in other

cases of progressive cicatrizing conjunctivitis such as ocular mucous membrane pemphigoid, lid surgery is known to exacerbate local inflammation and candidates often undergo a period of perioperative immunosuppression in hopes to control inflammation.<sup>15</sup>

Whilst cicatricial scarring resulted in poor visual outcome for our patient, fortunately with systemic immunosuppressive therapy our patient has achieved systemic disease remission with normalised kidney function. Further close monitoring and maintenance treatment will likely be required given the high likelihood of systemic disease relapse in ANCA associated vasculitis patients.<sup>16</sup> Given the previously reported association between tarsal-conjunctival disease and subglottic stenosis,<sup>10</sup>, our patient has also been referred to otorhinolaryngology for further assessment.

#### 4. Conclusion

Cicatricial entropion is a rare disease manifestation of GPA which typically follows a slow course of progressive scarring unaffected by systemic immunosuppressant therapy. Whilst the underlying pathophysiology of GPA is still unclear, we believe that surgical intervention may potentially induce rapid cicatricial disease progression with resultant significant poor outcomes. As a result, we would advised that any cases of cicatrizing conjunctivitis under consideration for lid surgery be met with a thorough systemic evaluation with the hopes of preventing late diagnosis of an underlying systemic inflammatory disease process.

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